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Sample Size Calculation Guide - Part 6: How to calculate the sample size for a non-inferiority or an equivalence clinical trial

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Introduction

In the previous educational articles, we explained how to calculate the sample size for a rate or a single proportion, for an independent cohort study, for an independent case-control study, for a diagnostic test accuracy study, and for a superiority clinical trial (1-5). In this article, we will explain how to calculate the sample size for a non-inferiority or equivalence clinical trial.

When to use the sample size calculation procedure of a non-inferiority or an equivalence trial

The methods explained hereafter should be used in case of a non-inferiority trial designed to prove than one intervention is not inferior to the other or an equivalence trial designed to prove that one intervention is equivalent to the other.

Requirements

1) Expected effect size (ES)
2) Type of clinical trial: Cross over or parallel
3) Allocation ratio between the experimental and control groups
4) Statistical power
5) Alpha
6) Margin of non-inferiority or Margin of equivalence

The expected effect size differs according to the type of outcome measure. In case of continuous measures, the required ES will be (1) the expected mean difference between the two arms and (2) the standard deviation of the mean difference. In the case of binary outcomes (events as death or remission), the required ES will be the expected rate of event each group.

Calculation steps

1) Open SampSize application on your mobile
2) Select superiority from the type of trial (superiority, non-inferiority, or equivalence)
3) Select parallel for the design of the study (parallel or cross over)
4) Select normal for the type of outcome data (normal or binary)
5) Put the data into space and click "calculate."

Case study of disease activity guided dose reduction of anti-TNF compared with usual care for patients with Rheumatoid arthritis

Assume that we are conducting a non-inferiority randomized controlled trial to compare the disease activity guided dose reduction (DR) versus usual care (UC) for patients with Rheumatoid arthritis. The alternative hypothesis of this study is that disease activity guided dose reduction is not inferior to the usual care. In the recent study Bouman et al. (6) reported 17% and 14% incidence rate of major flare after 3 years for the DR and UC groups, respectively. Assuming a non-inferiority margin of 20% difference in major flares, calculate the required sample size to detect similar ES.

Case solution

First, we determine the requirements

- Expected proportion of major flare in the two groups after 3 years
- Type of clinical trial: parallel
- Allocation ratio between the experimental and control groups = 1
- Statistical power = 90%
- Alpha = 5%
- Non-inferiority limit = 20%

Second, we run the calculations as shown in Figure 1. The results show that a minimum sample size of 156 patients (n=78 per group) will be required for this randomized controlled trial (Figure 1).

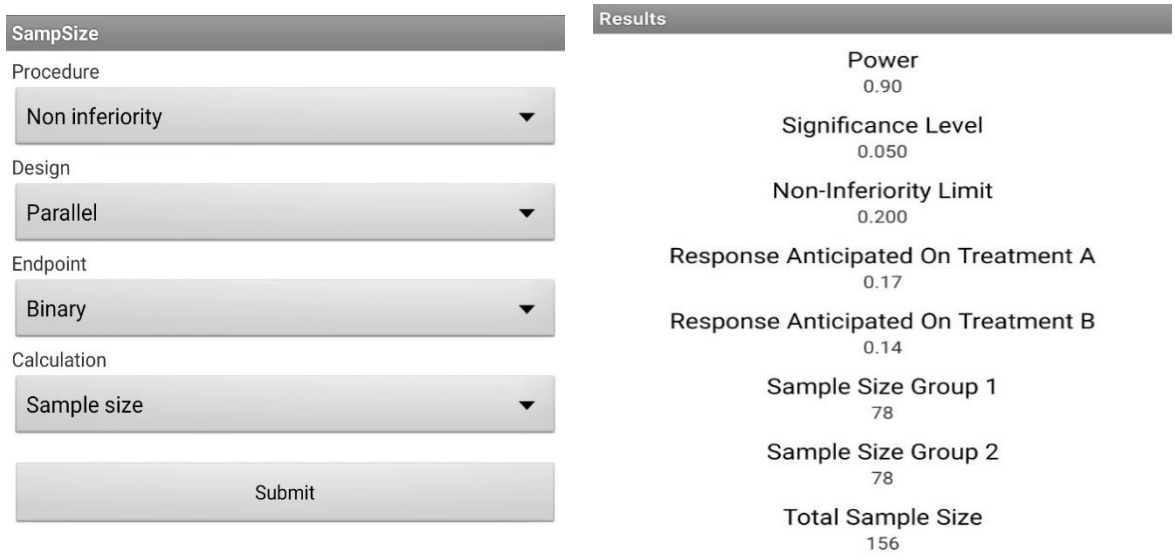

Figure 1: Calculating the sample size for a non-inferiority clinical trial using an application

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